DEPARTMENT OF HEALTH & HUMAN SERVICES

New York District

Food & Drug Administration
158-15 Liberty Avenue
Jamiaca, NY 11433

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mark A. Stern
President
Eight In One Pet Products, Inc.
2100 Pacific Street
Hauppauge, NY 11788-4737

June 14, 2002

Ref: NYK-2002-36

Dear Mr. Stern:

During an inspection of your drug manufacturing facility located in Hauppauge, New York, conducted between the dates of May 14 and 24, 2002, our investigator documented deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). Such deviations cause your drug products, including piperazine citrate syrup for dogs and cats, sulfadimethoxine solution for birds, and aspirin tablets for dogs, to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act as follows:

1. Failure to conduct a thorough investigation of unexplained discrepancies or the failure of a batch or any of its components to meet any of its specifications. [21 CFR 211.192]. There is no written investigation of piperazine citrate syrup, batch # 0421054 failure to meet assay specifications. The investigation of piperazine citrate raw material lot 20268 out of specification test results included retesting of new samples which was not thoroughly justified.

2. Failure to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process materials and drug products. [21 CFR 211.110]. There is no process validation data for drug products.

3. Failure to establish a written testing program designed to assess the stability characteristic of drug products. [21 CFR 211.166]. The inspection found that aspirin batches, for example, #s, 0320940 and 0421288, were labeled with a three year expiration date without the supporting stability data. Aspirin batches, for example, #s, 0421287 and 0220404, had no expiration date on the label. [21 CFR 211.137].

4. Failure to establish written specifications for active ingredient and excipient components used in drug products. [21 CFR 211.160]. The inspection also found that tap water is used as an ingredient in drug products. There are no written specifications and no test reports for this drug component. Your firm does not have a water treatment system to produce purified water.

5. Failure to follow written plans for sampling of drug components. [21 CFR 211.160]. The inspection found that only one container per lot of component is sampled, whereas, the written plan requires sampling from the square root plus one container.

6. Failure to have an individual inventory record of each component and a reconciliation of the use of each lot of such component. [21 CFR 211.184(c)].

7. Batch production records fail to include complete information relating to the production and control of batches. [21 CFR 211.188]:

a. The weights of all components actually used in the course of processing are not recorded on all batch records.

b. Failure to document each significant step in the manufacturing of each batch. Specific mixing speeds, times, and equipment are not always documented. The percentages of yield at all appropriate phases of processing are not documented. The batch records do not include records of sampling.

8. Failure to verify the suitability of all testing methods under actual conditions of use. [21 CFR 211.194]. There are no records of test method validation to assure accuracy and reliability. The adequacy of the contract testing laboratory has not been established, such as, by audit. [21 CFR 211.22]:

a. Examination of the raw data from the contract testing lab used for the testing of piperazine citrate syrup found that the specific gravity was not used in the final calculation as required by USP.

b. HPLC chromatograms from testing aspirin powder were found to have poor separation between active ingredient peak and an unknown peak, as well as, widely different retention times for the active peak between different chromatographic runs.

c. HPLC chromatograms from testing sulfadimethoxine found poor separation of the active peak, with shoulder and interfering peaks.

d. HPLC chromatographic data do not always document system suitability requirements.

e. There is no stability data and written procedures for the use of reference standard dilutions which are stored and not prepared just prior to their use in sample analysis.

9. Failure to maintain complete records of the periodic calibration of laboratory instruments. [21 CFR 211. 194]. There are no calibration records for the HPLC equipment.

10. Failure to clean and maintain equipment at appropriate intervals to prevent malfunctions or contamination. [21 CFR 211.67]. Layers of chemical powders were observed covering the lids of mixing tanks and equipment. Cleaning procedures have not been validated to assure the adequacy in preventing contamination.

11. Failure to maintain a written record of equipment cleaning, maintenance, and use that includes the date and time of usage. [21 CFR 211.182].

12. Failure to have documented review and approval of changes to procedures and controls. by the appropriate organizational unit and quality control. [21 CFR 211.100 & 211.160]. For example, there is no documented justifications or formal review of the changes to the formulation of aspirin tablets. Test methods are changed by cross outs without documented justifications.

We acknowledge receipt of Ms. Fareria's letter of June 4, 2002 which describes your firm's actions relating to the Inspectional Observations issued to you on May 24, 2002. The letter also questions FDA's analysis of a sample from a batch of piperazine citrate syrup. Compliance Officer Laurence D. Daurio's letter dated June 10, 2002 responded to Ms. Fareria regarding the FDA sample analysis.

With regard to the Inspectional Observations, Ms. Fareria states that Eight In One Pet Products is committed to correcting all items on the form FDA 483 and is adding new equipment and personnel, however, we note that your letter of November 19, 2001, responding to Inspectional Observations issued on October 3, 2001 after the previous inspection of your firm, also promised corrections. Despite being advised by Mr. Daurio's letter of December 31, 2001 that the promised changes and new procedures described in the November 2001 letter should be implemented promptly, our most recent inspection found continuing violations of CGMP regulations. The June 4, 2002 response letter is general, nonspecific, and includes no documentation of corrections. The letter also states that corrections would not be completed until October 2002. This delay is unacceptable if products are continued to be shipped. We request a more specific response at this time.

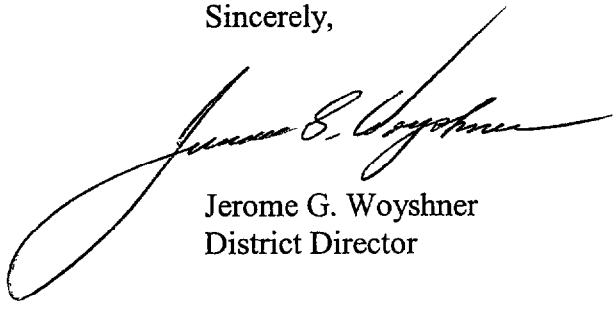
The above identification of violations and the observations on the form FDA-483 issued at the end of the inspection are not intended to be an all-inclusive list of violations. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include seizure and/or injunction.

You should notify this office in writing, within 15 working days of the receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for delay and the time within which corrections will be completed.

Your reply should be sent to Compliance Branch, Food and Drug Administration, New York District, 158-15 Liberty Avenue, Jamaica, NY 11433, Attention: Laurence D. Daurio, Compliance Officer.

Sincerely,



Jerome G. Woyshner
District Director